Recalcitrant asthma in a patient with nasal polyps, sinusitis, and aspirin-exacerbated respiratory tract disease

SEARCH AGAIN

Q:

7/9/2013

I recently saw a 33 year-old male with severe persistent asthma with an allergic component, perennial allergic rhinitis (with springtime allergic conjunctivitis), AERD. At the first visit, he had been recently discharged from ICU after intubat for asthma, the sixth intubation in the eight years since asthma diagnosis. Asthi triggered by pollens and aspirin, and is worse in the winter (possibly due to dus allergy as listed below).

The second visit, two weeks later, his nasal polyposis was increasingly symptom with large bilateral polyps and increased sinus pressure. Symptoms responded Prednisone and antibiotics (he felt better when I called to follow up after 1 week is maintained on Symbicort, Singulair, and Spiriva (prescribed by pulmonologis and Prednisone tapers when needed. He was using Symbicort 80/4.5 mcg two p once daily when he last got hospitalized. I increased this to 160/4.5 mcg two pu twice daily.
FEV1 was 75% predicted.

Total IgE was 144 IU/mL, and IgE to D. pter was 4.12 kU/L, D. farinae 4.32 kU/ Kentucky Bluegrass 0.13 kU/L.

There was no eosinophilia on recent CBC (performed off of Prednisone).

My question regards further treatment approach/timing- I would like to treat h with Omalizumab first. I think he may also benefit from aspirin desensitization the AERD component. My inclination would be to start with Xolair to hopefully control the asthma better, and then refer him to an academic center for the aspi desensitization. At some point, assuming asthma control is achieved, I would he offer immunotherapy. Would this be the order in which you would approach thi

A:

Thank you for your inquiry.

I do agree with the addition of omalizumab and the consideration of aspirin desensitiza also consider adding beclomethasone HFA to the treatment regimen since we know tha obstruction can contribute to exacerbations. In addition, I would also consider switchin montelukast to zileuton. However, because of his expertise and some very exciting rec in the area of aspirin-exacerbated respiratory tract disease, as well as his extensive cli experience in patients such as the one you described, I am asking Dr. Larry Borish for potential treatment strategies in your patient, especially in regards to the suggestion r switch from montelukast to zileuton. As soon as we receive Dr. Borish's response, we v to you.

Thank you again for your inquiry.

Sincerely,
Phil Lieberman, M.D.

We have received a response from Dr. Larry. Thank you again for your inquiry and we response is helpful to you.

Sincerely,
Phil Lieberman, M.D.

Response from Dr. Larry Borish:
On my 1st reading of this case I assumed this was a straightforward question about se someone with AERD. On further reading I think this is much more a case where the wh of asthma is worthy of being questioned. Between the 6 intubations and the no eosinop sure what this really is with the info given. So, half this paper has become a discussion importance of questioning diagnoses including asthma, nasal polyps, aspirin allergy, et

briefly we delve into the AERD comments. But I wouldn't give this patient xolair let alone aspir
desensitization without being a lot more convinced that he has asthma, polyps, etc., etc.

Hope you are happy with this approach!

Larry Borish, M.D.

Detailed response from Dr. Larry Borish:
When dealing with a particularly severe asthmatic - and there is nothing more compellingly se
than someone requiring intubation on 6 separate occasions who was clearly not responding to
whatever therapeutics were being provided at the time of those intubations - the first consider
has to be certainty of the diagnosis. Asthma is itself a collection of heterogeneous diseases tha
also masquerade as a multitude of other diagnoses. Obesity, vocal cord dysfunction, dysfunctio
breathlessness, severe reflux with aspiration, COPD, congestive heart failure, any many more
conditions can all mimic the presentation of asthma, leading to the quagmire that we know as
"asthma" today[1]. The patient in this vignette is on medium dose inhaled corticosteroids for a
presumed diagnosis of asthma and with laboratory evidence of sensitization to allergens. There
history of reported allergy to aspirin and, on physical exam, nasal polyps were observed. On th
surface, the may seem to be a straightforward presentation of Aspirin Exacerbated Respiratory
Disease (AERD). However, before delving into a discussion of the management of AERD, it see
each facet of this presentation needs to be scrupulously reconsidered. Especially before consid
expensive life-long interventions that might not be helpful, the initial approach to this - or any
patient with severe, potentially life-threatening, and seemingly steroid resistant asthma must i
a thorough examination of the data and further testing to confirm the diagnosis.

In the patient above, the limited history can provide some important clues as to the diagnosis.
Simply knowing that the patient has been intubated 6 times in 8 years gives the clinician insta
trepidation. In uncomplicated asthma, this is a rather unusual history. Amongst conditions that
masquerade as asthma, it is patients with vocal cord dysfunction who are much more regularly
intubated - because of the apparent severity of their presentations[2]. A quick survey of our own
experience includes many physicians and EMT's who have intubated patients who "look like the
tire out soon." However, few of these patients have objective evidence of tiring. At the very lea
should include arterial blood evaluation as, for truly asthmatic patients requiring intubation, th
would uncover an elevated (or rising pCO2) and - in contrast to VCD - an elevated Arterial-alve
pO2 gradient. Further investigation into hospital ventilator records would reveal the high lung
pressures and low lung volumes defining the poor pulmonary compliance of asthma, in contras
normal compliance seen in VCD.

For this patient, the only information we have supporting the diagnosis of obstructive lung dise
a slightly low FEV1. However, isolated, the significance of this finding is unclear. Of course, the
diagnosis of obstruction cannot be entertained without information regarding FVC and repeat
spirometry after bronchodilator will address the question of reversibility. It is important to rem
that everything with a low FEV1 is not asthma, as numerous considerations including poor tech
obesity, COPD, and numerous others can consistently mimic this finding. Ultimately, the gold
standard for diagnosis of asthma remains the methacholine challenge. In the absence of comp
information not provided in this brief vignette, arguably all patients with seemingly severe, ste
resistant asthma and with an FEV1 > 70% who have these sorts of inconsistencies in their
presentation should undergo a methacholine challenge.

The reported presence in this patient of nasal polyposis (NP) does seem supportive of the diag
asthma, something present in many if not most NP patients. It should be noted how this diagn
was made as on anterior rhinoscopy many anatomical variants (e.g., a deviated septum with a
visualizable middle turbinate) are often misconstrued to be a NP. Typically this diagnosis is bes
via rhinoscopy although significant hyperplastic disease observed on a sinus CT can strongly su
the diagnosis of NP (and - when present - the likelihood of concomitant asthma[3].

Once confirming the diagnosis of CRSwNP and asthma, it is the reported history of "sensitivity"
aspirin that suggests AERD - Samter's triad. However, like everything else in the realm of seve
asthma, the diagnosis of AERD can be difficult. This diagnosis is best supported by a compellin
history of upper and/or lower respiratory compromise in response to aspirin (or other NSAID)
occurring on two separate occasions[4]. Again, this history can be deceiving, as many people wh
consider themselves allergic to aspirin are simply describing the natural circadian history of the
asthma. And, alternatively, ASA/NSAID-induced exacerbations of GERD may trigger upper and
airways symptoms in the absence of AERD. Importantly, a history of urticaria/angioedema afte
taking aspirin is emphatically not associated with the diagnosis of AERD, and these patients sh
diagnosed and treated differently. Unambiguous confirmation of aspirin allergy is nearly impos
the absence of direct aspirin challenge, as it is not IgE mediated, and, therefore, there are no s
blood tests that are diagnostic. Recent studies suggest that a nasal ketorolac challenge is effec
determining who is allergic to aspirin[5].

There is one striking finding in this vignette that most places in doubt the diagnosis of AERD (i
asthma) and that is the absence of eosinophilia at a time when the patient was not on corticos
Peripheral eosinophilia is a cardinal feature of AERD, and a patient without this lab finding almo
certainly does not have this disease[6, 7]. It is certainly possible to have asthma without periphe
for that matter airway) eosinophilia however this is not seen in AERD.

AERD patients have particularly severe CRS sinus CT will reveal severe, nearly opacified sinuse
CT 8. It is also interesting that this patient was atopic. Allergy is not a feature of AERD[9, 10, 11]
when present this is likely just the concomitant presence of an unrelated but common phenoty

For a patient (probably not the one in this vignette) who does have AERD, after the presence c
polyps is confirmed by CT scan or rhinoscopy, a "medical polypectomy," is the initial approach.
"medical polypectomy" is defined as a steroid taper over ~21 days. This will only provide tran
relief but after shrinking the polyps and hopefully reopening the sinus ostia, saline rinses with
addition of a topical corticosteroid such as budesonide can be started[12]. Generally, repeat rhin
after the "medical polypectomy" can be useful to determine if the treatment was successful. If
not effective, surgical intervention is required. Patients with AERD are occasionally helped by
leukotriene receptor antagonists but for yet unclear reasons these patients may be uniquely
responsive to the 5-lipoxygenase inhibitor, zileuton[13]. As a single intervention in AERD, this ag
shrink polyps, improve sinus symptoms, markedly improve asthma, and - in over half the patie
restore sense of smell. If these approaches fail, the next consideration would be aspirin
desensitization[4, 14]. We prefer to do this shortly after surgery (within four weeks) both becaus
aspirin desensitization seems to work better to prevent regrowth of polyps than to eliminate
established disease and it is also our experience that removal of the sinus tissue mitigates the
of leukotrienes produced during the desensitization and makes for a safer procedure. Aggressi
medical management must be continued after surgery and aspirin desensitization, likely includ
zileuton and topical corticosteroid-containing saline nasal rinses, to retard the growth of polyps

For the concerns discussed, the use of omalizumab in this patient is debatable, and it would re
many of the tests delineated above to determine its appropriateness. If this patient truly has
allergen-exacerbated asthma (with or without concomitant AERD) then, in the presence of his
mite allergy, omalizumab might decrease future exacerbations and hospitalizations. But again,
first approach for this patient is to rule out a masquerading diagnosis such as obesity, vocal co
dysfunction, COPD, etc. and subsequently, to focus on a treatment plan unique for AERD - if th
similarly confirmed - as in our experience IgE sensitivities have modest impact in that conditio
Finally, the use of antibiotics for this patient's chronic sinusitis is also controversial, and recent
studies suggest that antibiotics may actually be detrimental in many patients[15, 16].

Larry Borish, MD
Professor of Medicine
University of Virginia Health Systems
Charlottesville, VA

Joshua Kennedy, MD
Assistant Professor of Pediatrics
University of Arkansas Medical Sciences
Little Rock, AR

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